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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,753	12/17/2001	David I. Watkins	960296.95874	8557

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EXAMINER	
LI, QIAN J	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 03/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,753	WATKINS ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply* .

DETAILED ACTION

Claims 1-14 are pending in the application and under current examination.

Priority

This application is a 371 of PCT/US00/00286, filed 1/6/2000, and claims benefit of priority from US provisional application 60/115,405, filed 1/8/1999.

Specification

The specification contains amino acid sequences (SEQ ID Nos: 1-6) that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures. Applicant must provide a paper copy and a computer readable copy of the Sequence Listing and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). A full response to this Office action must include a complete response to the requirement for a Sequence Listing.

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

Claim 1 is objected to because the word "histocompatibilty" in line 15 is mis-spelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims are vague and indefinite because claim 1 provides a method of inducing an epitope-specific CTL response in a primate, which encompasses a CTL-response to any epitope. The method comprises delivering polynucleotides encoding multiple epitopes including any viral polyepitope, an HBcAg epitope, and a MHC class I-restricted peptide epitope. However, it is unclear *which* epitope the phrase in the preamble, "the *epitope*-specific CTL" refers to, and which epitope the CTL specifically targets, i.e. the intended vaccine to be developed, thus, the metes and bounds of the claims are unclear.

Claim 1 further recites, "in an amount sufficient to induce in the primate a cytotoxic T lymphocyte response *specific for the MHC class I-restricted peptide epitope*. In light of the knowledge in the art, delivery of multiple epitopes would induce a response against every epitope administered, thus, it is unclear why the delivery of a

complex epitope vaccine induces a CTL-response only to the MHC class I-restricted epitope but not other epitopes. In light of the specification, it seems that applicants intend to develop a vaccine to HIV infection; therefore, for the sake of a compact prosecution and examination, the recited "viral polyepitope" is considered as the intended vaccine to be developed.

Claim 1 is vague and indefinite because it recites, "the sequences encoding" in line 11. The subject being encoded is missing, it is unclear which sequence the phrase is refer to or what protein the sequence encoding; if it refers to both sequences in (1) and (2), the inter-relation of the sequences and the promoter is unclear, whether they each linked to a promoter or they both linked to the same promoter, thus, the metes and bounds of the claims are unclear.

Claim 1 is vague and indefinite because of the claim recitation, "a major histocompatibility complex class I-restricted peptide epitope". The specification fails to define the term in general, it is unclear what peptide epitope the claims intend to embrace, and thus, the metes and bounds of the claims are unclear. In view of the teachings of *Ganeway et al*,(Immunobiol c2001) and for the sake of compact prosecution, the term would be interpreted as any peptide epitope that could stimulate a CTL response, including synthetic peptides (Section 14-23), tumor (Section 14-12), and viral epitopes (Section 11-25 and 11-26).

Claim 10 recites the limitation "the primate's viral load". There is insufficient antecedent basis for the limitation in the claim. Particularly, claim 10 depends from claims 2 and 1, and provides a further step of exposing a primate to a (any) virus.

Claims 1 and 2 are drawn to administering multiple compositions comprising multiple polynucleotides encoding any viral polyepitope, an HBcAg viral epitope, and a MHC class I-restricted peptide epitope derived from any virus; and claim 10 provides another step of exposing the primate to a (any) virus. It is unclear which virus the term "viral load" refers to, and it is unclear whether the type of the virus used in claim 10 is the same or different from one of the viral types administered in claims 1 and 2, thus, the metes and bounds of the claims are unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inducing an epitope-specific CTL *against a viral infection* associated with a viral polyepitope in a primate by delivering (1) a polynucleotide vector encoding a viral polypepitope with a MHC class I-restricted epitope (a CTL epitope) and (2) a polynucleotide encoding HBcAg and the CTL epitope, wherein the CTL epitope is derived from the *same* type of virus as said viral polyepitope, does not reasonably provide enablement for inducing an epitope-specific CTL against *any* antigenic epitope or against a viral infection associated with a viral polyepitope in a primate by delivering a viral polyepitope with a MHC class I-restricted epitope, wherein the CTL epitope is derived from a different type of virus or is derived from a tumor epitope. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention are summarized in *In re Wands*, (858 F2d 731, 737, 8 USPQ 2d 1400, 1404, (Fed Cir.1988)). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, the breadth of the claims, and amount of direction provided. The factors most relevant to this rejection are the scope of the claims relative to the state of the art and the levels of the skilled in the art, and whether sufficient amount of direction or guidance are provided in the specification to enable one of skill in the art to practice the claimed invention.

The claims are drawn to a method for inducing an epitope-specific CTL against any epitope with viral polyepitopes and CTL-epitopes from a viral or a tumor; in light of the specification, a preferred embodiment is a method for inducing an epitope-specific CTL against a viral infection in a primate by delivering a vaccine comprising a viral polyepitope with a CTL epitope derived from a virus or from a tumor epitope. Given the broadest reasonable interpretation, the CTL epitope could be any type of virus, which is the same or different from the viral polyepitope; and the CTL epitope could be any type of tumor. The claim recites the resolution of the method as, "in an amount sufficient to induce in the primate a cytotoxic T lymphocyte response specific for the major histocompatibility complex class I-restricted peptide epitope", accordingly, when the

MHC class I-restricted epitope is derived from a tumor, the induced response would be specifically against a tumor epitope; and when the CTL epitope is derived from a virus that differs from said viral polyepitope, the induced response would be specifically against the virus from which the CTL epitope derived, not the polyepitope the vaccine intended to target. The specification teaches delivering a recombinant polynucleotide encoding an HIV polyepitope and a CTL epitope derived from HIV epitope, and an HBV core antigen, here, the polyepitope and the CTL epitope are derived from the same type of virus, and the synergistic vaccine effects results in a protective immune response against HIV in rhesus macaques. The specification also teaches that hepatitis B core antigen is known to be used as a carrier moiety to enhance both humoral and cellular immune responses of a foreign pathogenic epitopes. However, the specification is silent regarding the situations where the CTL epitope and the viral polyepitope are derived from different types of viruses or a different type of antigen, such as tumor. Likewise, the specification is silent regarding whether using viral polyepitopes and a CTL-epitope derived from a tumor could elicit an effective response specific for tumor CTL-epitope.

It is well known in the art, the immune system responds in distinct and specialized ways to different types of antigens (*Abbas et al*). An anti-viral immune response differs from an anti-tumor response in many ways even though a CTL may be involved in both responses as an effector cell. While the immune response against infectious agent such as a virus is part of the natural defense function of an immune system, the etiology and mechanism of anti-tumor response is still under investigation, and immune responses frequently fail to prevent the growth of tumors, thus, the effects

of tumor CTL epitope on combating the viral infection or vice versa is not known and unpredictable. The specification fails to teach the overall effects of combining a tumor antigen with a viral antigen on the efficacy of an anti-viral or anti-tumor response, thus, fails to provide sufficient enabling disclosure to support the full scope of the claims.

Therefore, in view of the limited guidance, the lack of predictability of the art and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b). (8.33)

The reference patent application qualifies as prior art under this provision because there is one common inventor and no common assignee between the instant application and the cited patent.

Claims 1 and 2 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19 and 20 of

copending Application No. 09/434,830. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 19 and 20 of copending Application No. 09/434,830 embrace the instant claims.

Claims of the present and copending applications are each drawn to a process of inducing a cellular immune response in a subject comprising delivering into cells of the subject two recombinant polynucleotides encoding an antigenic epitope, wherein one of the recombinant polynucelotides is a hepatitis B core antigen carrier.

The processes of each application differ one from the other in that the claims of instant application particularly drawn to a primate as a subject, a viral polyepitope as the target antigen, however, the subject matters are fully embraced by the cited application. The processes of each application further differ one from the other in that the claims of instant application comprise a booster regimen. However, including a booster dose in vaccination is fully taught by the cited application (page 5, 2nd paragraph).

Accordingly, the claimed processes in the copending and the present applications are obvious variants. Therefore, the inventions as claimed are co-extensive.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (f) he did not himself invent the subject matter sought to be patented.

The reference patent application qualifies as prior art under this provision because there is at least one common inventor and no common ownership currently between instant and the cited applications.

Claims 1 and 2 are provisionally rejected under 35 U.S.C. 102(e) as being anticipated by copending Application No. 09/434,830 which has two common inventors with the instant application. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e), if published under 35 U.S.C. 122(b) or patented. This provisional rejection under 35 U.S.C. 102(e) is based upon a presumption of future publication or patenting of the copending application.

Claims 1 and 2 of the present application and claims 19 and 20 of the copending application are each drawn to a process of inducing a cellular immune response in a subject comprising delivering into cells of the subject two recombinant polynucleotides encoding an antigenic epitope and a CTL epitope, wherein one of the recombinant polynucleotides is a hepatitis B core antigen carrier.

The processes of each application differ one from the other in that the claims of instant application are particularly drawn to a primate as a subject, a viral polyepitope as the target antigen, however, the subject matters are fully embraced by the cited

application. The processes of each application further differ one from the other in that instant method steps comprise a booster dose of a viral vector expressing the antigen. However, including a booster dose in vaccination is fully disclosed in the cited application (e.g. 2nd paragraph, page 5). Therefore, the cited application anticipate the instant claims.

This provisional rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131. This rejection may not be overcome by the filing of a terminal disclaimer. See *In re Bartfeld*, 925 F.2d 1450, 17 USPQ2d 1885 (Fed. Cir. 1991).

Claims 1 and 2 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter. As discussed in the immediate preceding rejection, the process of instant claims 1 and 2 is anticipated by the cited patent application, however, the inventive entities are different between two applications. Further clarification is required regarding who is the inventor for the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Fuller et al* (Immunol Cell Biol 1997;75:389-96) and *Fuller et al* (Vaccine 1997;15:924-5), in view of *Hanke et al* (J Gen Virol 1998 Jan;79:83-90), *Borgne et al* (Virol 1998;240:304-15), and further in view of *Loktev et al* (J Biotechnol 1996;44:129-37).

The claims are drawn to a method of inducing an epitope specific CTL response in a primate including a human comprises the step of (a) delivering into cells of the primate a polynucleotide vaccine comprising (1) a polynucleotide sequence encoding a viral polyepitope and a MHC class I-restricted peptide epitope, and (2) a polynucleotide sequence encoding a hepatitis B core antigen and a MHC class I-restricted peptide epitope, the sequences are operably linked to a promoter, wherein the vaccine is preferably delivered by particle bombardment or any type of injection. The method further comprises a booster step (b) delivering a live virus vector comprising a polynucleotide sequence encoding a viral polyepitope and a MHC class I-restricted peptide epitope, wherein the a MHC class I-restricted peptide epitope is a viral epitope, an HIV polypeptide selected from the group consisting of HIV gag, pol, nef, tat, rev, and env; wherein the step (a) is repeated at least once prior to step (b), wherein the step (b)

is repeated at least once and CTL response is increased relative to the response induced by step (a); wherein the primate is subject to a virus challenge after step (b), and the primate's viral load is lower compared to the controls, wherein the CTL is detectable by tetramer staining of fresh unstimulated polymorphonuclear blood cells (PMBC), wherein the fresh PMBC of the vaccinated primate produce interferon-g after step (a).

The first reference of *Fuller et al* teaches a gene gun-based (particle bombardment) nucleic acid vaccination method for SIV in a primate (rhesus macaques) combined with a live recombinant vaccinia viral vector comprising a polynucleotide sequence expressing SIV env epitope (gp160) as a booster immunization (abstract). Before receiving the booster dose of the vaccinia virus (DNA+VAC), the rhesus macaques received seven consecutive doses of the nucleic acid vaccine expressing an env polypeptide of SIV (gp120 and gp160) driven by a CMV intron A promoter (Expression vectors, page 390), and certain group of macaques received more than one vaccinia virus (VAC+VAC). In the subsequent challenge with infectious doses of SIV (comprising the epitope of gp120 and gp160), all vaccine groups showed significant reduction in SIV virus load when compared to controls. *Fuller et al* go on to teach that using repeated DNA immunization alone would lead to a significant decline in antibody response to virus, and this may be overcome by combining DNA priming with protein or recombinant vaccinia virus boosts (paragraph bridging pages 393-4).

The second reference of *Fuller et al* elaborates the teachings of the first one, and teaches that in contrast to DNA vaccination for influenza and hepatitis B, DNA plasmids

coding for antigens from SIV and HIV have elicited relatively weak antibody responses, but boosting gene gun-primed animals with either recombinant subunits or gp120-expressing recombinant vaccinia virus could achieve synergistic responses (abstract) and dramatically improve antibody response (Section in page 926). They teach DNA constructs expressing HIV env, or gag-pol-env (Section in page 925) as well as SIV (Section in page 924 and 926). The two *Fuller et al* references do not teach HBcAg or MHC class I-restricted peptide epitope.

Hanke et al teach to include a multi-CTL epitope (MHC class I-restricted peptide epitope) in the vaccine for HIV (abstract). They teach the importance of eliciting a CD8+ (cytotoxic T lymphocyte) response in the development of an HIV vaccine, and they construct a modified vaccinia virus Ankara (MVA) expressing multi-CTL epitope derived from immunodeficiency virus (a portion of an HIV env polypeptide) consisting of 20 human, one murine and three rhesus macaque epitope and administering the recombinant MVA into mice (H epitope, left column, page 84). They teach to include antigens from mice and macaques in order to conduct pilot study for an optimal vaccine regimen, such as optimal dosage and routes of administration, before a trial applied in humans. They delivered the vaccine by intravenous and intramuscular injection, and obtained specific CTL responses via both routes of administration (pages 86-87). Fig. 4 illustrates IFN-γ-producing cells upon stimulation with HIV epitope. Because the method steps and type of CTL and viral epitopes used in the cited reference are embraced by instant claims, the epitope-specific cytotoxic T lymphocyte response would be detectable by tetramer staining of fresh unstimulated polymorphonuclear blood cells,

and fresh unstimulated polymorphonuclear blood cells from these primates would produce IFN-γ. *Hanke et al* further tested the H epitope in cultivated human cells, and observed correct processing and presentation of H epitope in human cells (fig. 5). *Hanke et al* carried the experiments in mice and human cells, but not a primate.

Borgne et al teach inducing a specific CTL response to HIV in both mice and rhesus macaques with a DNA vector expressing an HIV epitope and a CTL-epitope fused with HBsAg. The DNA vector construct comprises a CMV promoter operably linked to the HIV env polyepitope coding region, a MHC class I-restricted epitope (IPQSLDSWWTSL), and a hepatitis antigen epitope (fig. 1), they obtained specific CTL responses to both HIV and HBV in mice as well as rhesus macaques (abstract, tables 2a+2b). *Borgne et al* do not use a hepatitis B core antigen but a hepatitis surface antigen.

Loktev et al teach various approaches to enhance the effectiveness of a molecular vaccine. They teach one of the known approaches is expressing a peptide in a special protein-carrier, such as HBsAg (paragraph bridging pages 129-30). *Loktev et al* go on to teach that the core antigen particles could also be used as a carrier and appears to be the most promising carrier exposing foreign epitopes compared to other means tested (1st & 2nd paragraphs under Discussion section).

Evidently, at the time of instant filing, using multiple dosing regimen and combining DNA vector with a viral vector in the HIV vaccination is well known in the art as taught by *Fuller et al*, enhancing a CTL response to HIV with multi-CTL epitope and a hepatitis core antigen carrier are also well known in the art as taught by *Hanke et al,*

Borgne et al, and *Loktev et al*; and it is also known that the CTL response to a polynucleotide encoding a HIV antigen, a multi-CTL epitope, and a hepatitis viral antigen are similar in mice and primates as taught by *Borgne et al.* Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Fuller et al,* by simply combining various approaches known in the art with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the different approaches would result in a synergistic effect in enhancing the CTL response, thus the HIV vaccine efficacy. Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Patent Examiner
Art Unit 1632

QL
March 10, 2003

Notice to Comply	Application No. 09869753	Applicant(s) Watkins et ak	
	Examiner Q. Janice Li	Art Unit 1632	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other:

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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